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# **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

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Sheet 1 of 4


Complete if Known	
Application Number	09/322,289
Filing Date	May 28, 1999
First Named Inventor	Dale B. Schenk
Group Art Unit	1647
Examiner Name	S. Turner
Attorney Docket Number	15270J-004740US

## **U.S. PATENT DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			

## **FOREIGN PATENT DOCUMENTS**

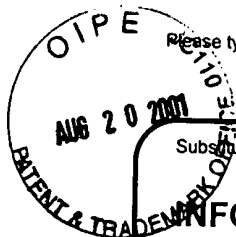
Examiner Initials *	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
70	47	EP	526 511	B1		05-28-1997		<input type="checkbox"/>
80	92	GB	2 220 211	A		01-04-1990		<input type="checkbox"/>

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SO	99	BORCHELT et al., "Accelerated Amyloid Deposition in the Brains of Transgenic Mice Coexpressing Mutant Presenilin 1 and Amyloid Precursor Proteins," <u>Neuron</u> , 19: 939-945 (1997).	<input type="checkbox"/>
	100	BORIS-LAWRIE et al., "Recent advances in retrovirus vector technology," <u>Cur. Opin. Genet. Develop.</u> , 3: 102-109 (1993).	<input type="checkbox"/>
	103	DUFF et al., "Mouse model made," <u>Nature</u> , 373: 476-477 (1995)	<input type="checkbox"/>
	104	ELIZAN et al., "Antineurofilament antibodies in a postencephalitic and idiopathic Parkinson's disease," <u>J. Neurol. Sciences</u> , 59:341-347 (1983).	<input type="checkbox"/>
	109	GAMES et al., "Alzheimer-type neuropathology in transgenic mice overexpressing V717F $\beta$ -amyloid precursor protein," <u>Nature</u> , 373(6514): 523-527 (1995).	<input type="checkbox"/>
	111	GASKIN et al., "Human antibodies reactive with beta-amyloid protein in Alzheimer's disease," <u>J. Exp. Med.</u> , 177:1181-1186 (1993).	<input type="checkbox"/>
	112	GLENN et al., "Skin immunization made possible by cholera toxin," <u>Nature</u> , 391: 851 (1998).	<input type="checkbox"/>
	113	GLENNER et al., "Alzheimer's Disease: Initial Report of the Purification and Characterization of a Novel Cerebrovascular Amyloid Protein," <u>Biochemical and Biophysical Research Communications</u> , 120(3): 885-890 (1994).	<input type="checkbox"/>
	114	GLENNER et al., "Alzheimer's Disease and Down's Syndrome: Sharing of A Unique Cerebrovascular Amyloid Fibril Protein," <u>Biochemical and Biophysical Research Communications</u> , 122(3): 1131-1135 (1984).	<input type="checkbox"/>
	117	GUPTA et al., "Differences in the immunogenicity of native and formalized cross reacting material (CRM197) of diphtheria toxin in mice and guinea pigs and their implications on the development and control of diphtheria vaccine based on CRMs," <u>Vaccine</u> , 15(12/13): 1341-1343 (1997).	<input type="checkbox"/>
	119	HANES et al., "New advances in microsphere-based single-dose vaccines," <u>Advanced Drug Delivery Reviews</u> , 28: 97-119 (1997).	<input type="checkbox"/>
	120	HARDY, "Amyloid, the presenilins and Alzheimer's disease," <u>TINS</u> , 20(4): 154-159 (1997).	<input type="checkbox"/>
	122	HSIAO et al., "Correlative Memory Deficits, A $\beta$ Elevation, and Amyloid Plaques in Transgenic Mice," <u>Science</u> , 274: 99-102 (1996).	<input type="checkbox"/>
	126	JANSEN et al., "Immunotoxins: Hybrid Molecules Combining High Specificity and Potent Cytotoxicity," <u>Immun. Rev.</u> , 62: 185-216 (1982).	<input type="checkbox"/>
SO	130	LANGER, "New Methods of Drug Delivery," <u>Science</u> , 249: 1527-1532 (1990).	<input type="checkbox"/>

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Sheet 3 of 4

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First Named Inventor	Schenk, Dale B.
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132	LEMERE et al., "Mucosal Administration of A $\beta$ Peptide Decreases Cerebral Amyloid Burden In Pd-App Transgenic Mice," <u>Society for Neuroscience Abstracts</u> , vol. 25, part I, Abstract 519.6, 29th Annual Meeting, (October 23-28, 1999).	<input type="checkbox"/>
133	LIVINGSTON et al., "The Hepatitis B Virus-Specific CTL Responses Induced in Humans by Lipopeptide Vaccination Are Comparable to Those Elicited by Acute Viral Infection," <u>J. Immunol.</u> , 159: 1383-1392 (1997).	<input type="checkbox"/>
134	LOPEZ et al., "Serum auto-antibodies in Alzheimer's disease," <u>Acta. Neurol. Scand.</u> , 84:441-444 (1991).	<input type="checkbox"/>
135	MCGEE et al., "The encapsulation of a model protein in poly (D, L lactide-co-glycolide) microparticles of various sizes: an evaluation of process reproducibility," <u>J. Micro. Encap.</u> , 14(2): 197-210 (1997).	<input type="checkbox"/>
138	NATHANSON et al., "Bovine Spongiform Encephalopathy (BSE): Causes and Consequences of a Common Source Epidemic," <u>Am. J. Epidemiol.</u> , 145(11): 959-969 (June 1, 1997).	<input type="checkbox"/>
140	PARECSE et al., "Microglial cells influence aggregates of the Alzheimer's disease amyloid beta-protein via a scavenger receptor," <u>Neuron</u> , 17:553-565 (September 1996).	<input type="checkbox"/>
141	PAUL et al., "Transdermal immunization with large proteins by means of ultradeformable drug carriers," <u>Eur. J. Immunol.</u> , 25: 3521-3524 (1995).	<input type="checkbox"/>
142	PRIEELS et al., "Synergistic adjuvants for vaccines," <u>Chemical Abstracts</u> , 120(8): pg. 652, column 1, abstract 86406t (1994).	<input type="checkbox"/>
145	RASO, "Immunotherapy of Alzheimer's Disease," <u>Immunotherapy Weekly</u> , Abstract (April 2, 1998).	<input type="checkbox"/>
149	SELKOE, D.J., "Imaging Alzheimer's Amyloid," <u>Nat. Biotech.</u> , 18:823-824 (2000).	<input type="checkbox"/>
150	SELKOE, "Alzheimer's Disease: A Central Role for Amyloid," <u>J. Neuropathol. Exp. Neurol.</u> , 53(5): 438-447 (1994).	<input type="checkbox"/>
151	SELKOE, "Physiological production of the $\beta$ -amyloid protein and the mechanism of Alzheimer's disease," <u>Trends in Neurosciences</u> , 16(10): 403-409 (1993).	<input type="checkbox"/>
156	SEUBERT et al., "Isolation and quantification of soluble Alzheimer's $\beta$ -peptide from biological fluids," <u>Nature</u> , 359: 325-327 (1992).	<input type="checkbox"/>
158	SMITS et al., "Prion Protein and Scrapie Susceptibility," <u>Vet. Quart.</u> , 19(3): 101-105 (1997).	<input type="checkbox"/>
159	SOLOMON et al., "Disaggregation of Alzheimer $\beta$ -amyloid by site-directed mAb," <u>PNAS</u> , 94:4109-4112 (1997).	<input type="checkbox"/>
160	SOLOMON et al., "Monoclonal antibodies inhibit <i>in vitro</i> fibrillar aggregation of the Alzheimer $\beta$ -amyloid peptide," <u>PNAS</u> , 93:452-455 (1996).	<input type="checkbox"/>
161	SOLOMON, A., "Pro-Rx (Protein Therapeutics)," University of Tennessee Medical Center (publication date unknown) <i>improper format</i>	<input type="checkbox"/>
163	STOUTE et al., "A Preliminary Evaluation of a Recombinant Circumsporozoite Protein Vaccine Against <i>Plasmodium Falciparum</i> Malaria," <u>N. Engl. J. Med.</u> , 336(2): 86-91 (1997).	<input type="checkbox"/>

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*S. Turner*

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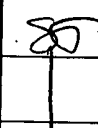

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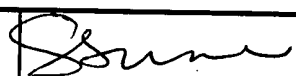
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First Named Inventor	Schenk, Dale B.
Group Art Unit	1647
Examiner Name	S. Turner
Attorney Docket Number	15270J-004740US

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	164	STURCHLER-PIERRAT et al., "Two amyloid precursor protein transgenic mouse models with Alzheimer disease-like pathology," <i>PNAS</i> , 94: 13287-13292 (1997).	<input type="checkbox"/>
	172	WEISSMANN et al., "Bovine spongiform encephalopathy and early onset variant Creutzfeldt-Jakob disease," <i>Curr. Opin. Neurobiol.</i> , 7: 695-700 (1997).	<input type="checkbox"/>
	173	WOOD et al., "Amyloid precursor protein processing and A $\beta$ 42 deposition in a transgenic mouse model of Alzheimer disease," <i>PNAS</i> , 94: 1550-1555 (1997).	<input type="checkbox"/>
	174	Human Immunology & Cancer Program brochure, from The University of Tennessee Medical Center/ Graduate School of Medicine, Knoxville, Tennessee (publication date unknown). <i>Improper format</i>	<input type="checkbox"/>

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	283	09/441,140		Solomon et al.	11-16-1999	
	242	00/168,594		Chalifour et al.	N/A	
	282	00/169,687		Chain	N/A	
	295	00/184,601		Holtzman et al.	N/A	
	299	00/188,295		Rasmussen et al.	N/A	
	296	00/254,465		Holtzman et al.	N/A	
	297	00/254,468		Holtzman et al.	N/A	
	300	2001/0018053	A1	McMichael	08-30-2001	
	267	6,294,171	B2	McMichael	09-25-2001	
	234	6,284,221	B1	Schenk, et al.	09-04-2001	
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	284	5,231,170		Averback	1993-07-27	

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	294	PCT	01/62801	A2		08-30-2001		
	301	PCT	01/62284	A2		03-01-2000		
	298	PCT	01/42306	A2		06-14-2001		
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	240	PCT	00/43039	A1		07-27-2000		
	227	PCT	95/11008	A2		04-27-1995		

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SO	228	BARROW, et al., "Solution Conformations and aggregational Properties of Synthetic Amyloid Beta-Peptides of Alzheimer's Disease. Analysis of Circular Dichroism Spectra" <u>J. Mol. Biol.</u> , 225(4): 1075-1093 (1992)	
	229	HAZAMA, et al., "Intranasal Immunization Against Herpes Simplex Virus Infection by Using a Recombinant Glycoprotein D Fused With Immunomodulating Proteins, the B Subunit of Escherichia Coli Heat-Labile Enterotoxin and Interleukin-2", <u>Immunology</u> , Vol. 78: 643-649 (1993)	
	233	MORRIS, et al., "The Consortium to Establish a registry for Alzheimer's Disease (CERAD)," <u>Neurology</u> , 39:1159-65 (1989)	
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	225	Press Release, from Elan, "Elan and AHP Provide an Update on the Phase 2A Clinical Trial of AN-1792," (1/28/2002)	
SO	226	Press Release, from Elan, "Elan and Wyeth Provide Update on Status of Alzheimer's Collaboration," (3/1/2002)	
	220	<del>Dialog/Derwent, Abstract of WPI-Acc No.: 1997-054436/199706: Stable vaccine compsns. comprise a macrocyclic lactone, a milbemycin, an avermectin, an antigen, a dispersing agent, an adjuvant, a water-sol. organic solvent and saline or water, Derwent File 354: Derwent WPI database. (Publication date unknown)</del> <i>improper format</i>	
	222	<del>Chemical Abstract database, Abstract of "Injection of Newborn Mice with Seven Chemical Adjuvants to Help Determine Their Safety in Use in Biologicals," Chemical Abstract database. (Publication date unknown)</del> <i>improper format</i>	
	223	<del>Wisconsin Alumni Research Foundation, "Injection of Newborn Mice with Seven Chemical Adjuvants to Help Determine Their Safety in Use in Biologicals," U.S. Govt. Res. Develop. Rep.: 70(24):56. (Publication date unknown)</del> <i>improper format</i>	
SO	224	Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, Thimerosal in Vaccines (Mercury in Plasma-Derived Products), web site contents found at : <a href="http://www.fda.gov/cber/vaccine/thimerosal.htm">http://www.fda.gov/cber/vaccine/thimerosal.htm</a> , last updated May 16, 2002.	
	235	NEWCOMBE and COHEN, "Solubility characteristics of isolated amyloid fibrils," <u>Biochim. Biophys. Acta</u> , 104:480-486 (1965).	
	236	HILBICH et al., "Human and rodent sequence analogs of Alzheimer's amyloid $\beta$ A4 share similar properties and can be solubilized in buffers of pH 7.4," <u>Eur. J. Biochem.</u> , 201:61-69 (1991).	
	237	GORTNER, <u>Outlines of Biochemistry</u> , pp. 322-323, John Wiley & Sons, Inc., New York (1949)	
SO	238	MCNEAL et al., "Stimulation of local immunity and protection in mice by intramuscular immunization with triple- or double-layered rotavirus particles and QS-21," <u>Virology</u> , 243:158-166 (1998).	

Examiner Signature	<i>Sharon L. Turner</i>	Date Considered	10-6-03
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239	Beasley, "Alzheimer's traced to proteins caused by aging," Reuters, April 20, 2001 7:56 PM ET.
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Sheet 4 of 5

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Application Number	09/322,289
Filing Date	May 28, 1999
First Named Inventor	Dale B. Schenk
Group Art Unit	1647
Examiner Name	Sharon L. Turner
Attorney Docket Number	15270J-004740US

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Sheet 5 of 5

## Complete if Known

Application Number	09/322,289
Filing Date	May 28, 1999
First Named Inventor	Dale B. Schenk
Group Art Unit	1647
Examiner Name	Sharon L. Turner
Attorney Docket Number	15270J-004740US

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Application Number

09/322,289

Filing Date

May 28, 1999

First Named Inventor

Schenk, Dale B.

Group Art Unit

1647

Examiner Name

Turner, Sharon L.

Attorney Docket Number

15270J-004740US

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	302	CHUNG et al. "Uptake, Degradation, and Release of Fibrillar and Soluble Forms of Alzheimer's Amyloid $\beta$ -Peptide by Microglial Cells," <u>J. Biol. Chem.</u> , 274(45):32301-32308 (1999).	
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				Filing Date	May 28, 1999
				First Named Inventor	Schenk, Dale B.
				Art Unit	1647
				Examiner Name	Turner, Sharon L.
				Attorney Docket Number	15270J-004740US

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Filing Date	May 28, 1999
First Named Inventor	Schenk, Dale B.
Art Unit	1647
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Attorney Docket Number	15270J-004740US

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**U.S. PATENT DOCUMENTS**

Examiner	Cite No. <sup>1</sup>	Document Number Number Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	305	09/724,842	41-28-2000	Chalifour, et al.	not for publication
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	321	5,837,672	11-17-1998	Schenk et al.	
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		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	322	PCT	00/72880	A2, A3	12-07-2000			
	323	PCT	00/72876	A2, A3	12-07-2000			
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## Compleat if Known

Application Number	09/322,289
Filing Date	May 28, 1999
First Named Inventor	Schenk, Dale B.
Art Unit	1647
Examiner Name	Turner, Sharon L.
Attorney Docket Number	15270J-004740US

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SP	307	CHEN, et al. A learning deficit related to age and beta-amyloid plaques in a mouse model of Alzheimer's disease. Nature. 408(6815):975-9 (2000).	
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**Complete if Known**

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Filing Date	May 28, 1999
First Named Inventor	Schenk, Dale B.
Art Unit	1647
Examiner Name	Turner, Sharon L.
Attorney Docket Number	15270J-004740US

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Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
89	327	CAMERON, E., "Recent Advances in Transgenic Technology," <u>Molecular Biotechnology</u> , 7:253-265 (1997).	
	328	FELSENSTEIN et al., "Transgenic Rat and In-Vitro Studies of B-Amyloid Precursor Protein Processing;" <u>Alzheimer's and Parkinson's Diseases</u> , Hanin et al. Ed., pp 401-409, Plenum Press, New York, (1995).	
	329	NIEMANN, H., "Transgenic farm animals get off the ground;" <u>Transgenic Research</u> 7:73-75 (1998).	
85	330	SIGMUND, C., "Viewpoint: Are Studies in Genetically Altered Mice Out of Control," <u>Arterioscler Thromb Vasc Biol.</u> , 20:1425-1429 (2000).	

Examiner Signature		Date Considered	10-6-03
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Substitute for form 1449/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	09/322,289
		Filing Date	May 28, 1999
		First Named Inventor	Schenk, Dale B.
		Art Unit	1647
		Examiner Name	Sharon L. Turner
Sheet 1 of 1	Attorney Docket Number	15270J-004740US	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
SO	349	Check, "Battle of the Mind," <u>Nature</u> , 422:370-372 (March 2003).	
SO	350	Nicoll et al., "Neuropathology of human Alzheimer's disease after immunization with amyloid- $\beta$ peptide: a case report," <u>Nature Medicine</u> , 9(4):448-452 (April 2003).	

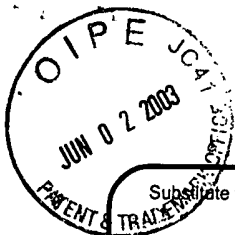
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Supplement for form 1449A/PTO

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STATEMENT BY APPLICANT**

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Sheet 1 of 3

**Complete if Known**

Application Number	09/322,289
Filing Date	May 28, 1999
First Named Inventor	Dale B. Schenk
Art Unit	1647
Examiner Name	Sharon L. Turner
Attorney Docket Number	15270J-004740US

**U.S. PATENT DOCUMENTS**

Examiner	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
SP	340	2002/0162129	A1	10-31-2002	Lannfelt	
	342	2002/0009445	A1	01-24-2002	Du et al.	
	345	2002/0077288	A1	06-21-2001	Frangione	
	346	5,935,927		08-10-1999	Vitek et al.	
	353	5,824,322		10-20-1998	Balasubramanian	
	357	5,776,468	B1	07-07-1998	Hauser et al.	
	356	5,622,701		04-22-1997	Berg	
	358	5,583,112	B2	12-10-1996	Kensil et al.	

**U.S. PATENT DOCUMENTS**

Examiner	Cite No. <sup>1</sup>	Document Number		Filing Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
SP	296	60/254,465		12-08-2000	Holtzman et al.	↑ NOT FOR PUBLICATION ↓
	297	60/254,498		12-08-2000	Holtzman et al.	
	305	09/724,842		11-28-2000	Chalifour et al.	
	295	60/184,601		02-24-2000	Holtzman et al.	
	282	60/169,687		12-08-1999	Chain	
	242	60/168,594		11-29-1999	Chalifour et al.	
	283	09/441,140		11-16-1999	Solomon et al.	
	299	60/186,295		03-01-2000	Rasmussen et al.	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
SP	352	WO	02/34777	A1	05-02-2002			
	351	WO	02/34878	A2	05-02-2002			
	343	EP	1 172 378	A1	01-16-2002			
	344	WO	01/90182	A2	11-29-2001			
	348	WO	01/77167	A2	10-18-2001			
	341	WO	02/03911	A2	04-07-2001			
	331	WO	99/06545	A2	11-02-1999			

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		Filing Date	May 28, 1999
		First Named Inventor	Dale B. Schenk
		Art Unit	1647
		Examiner Name	Sharon L. Turner
		Attorney Docket Number	15270J-004740US
Sheet	2	of	3

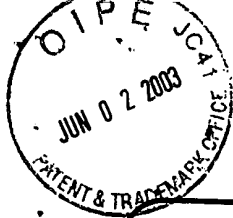
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4	332	CHEN et al., "Neurodegenerative Alzheimer-like pathology in PDAPP 717V→F transgenic mice," <u>Progress in Brain Research</u> , Van Leeuwen et al. Eds, 117:327-337 (1998).	
	333	CONWAY et al., "Acceleration of oligomerization, not fibrillization, is a shared property of both $\alpha$ -synuclein mutations linked to early-onset Parkinson's disease: Implications for pathogenesis and therapy," <u>PNAS</u> , 97(2):571-576 (2000)	
	334	JOBLING and HOLMES, "Analysis of structure and function of the B subunit of cholera toxin by the use of site-directed mutagenesis," <u>Molecular Microbiology</u> , 5(7):1755-1767 (1991).	
	347	JORBECK et al., "Artificial <i>Salmonella</i> Vaccines: <i>Salmonella typhimurium</i> O-antigen-Specific Oligosaccharide-Protein Conjugates Elicit Opsonizing Antibodies that Enhance Phagocytosis," <u>Infection and Immunity</u> , May:497-502 (1981).	
	335	MASLIAH et al., " $\beta$ -Amyloid peptides enhance $\alpha$ -synuclein accumulation and neuronal deficits in a transgenic mouse model linking Alzheimer's disease and Parkinson's disease," <u>PNAS</u> , 98(21):12245-12250 (2001).	
	359	MUNCH et al., "Potential neurotoxic inflammatory response to A $\beta$ vaccination in humans," (2002) <u>J. Neural Transm.</u> , 109:1081-1087.	
	355	MUNSON ed., "Principals of Pharmacology: Basic Concepts & Clinical Applications," (1995), 47-48, Chapman & Hall, New York, New York.	
	354	MUTSCHLER et al., "Drug Actions: Basic Principles and Therapeutic Aspects," (1995) 7, 11-12, <u>medpharm</u> Scientific Publishers, Stuttgart, Germany.	
	336	PERUTZ et al., "Amyloid fibers are water-filled nanotubes," <u>PNAS</u> , 99(8):5591-5595 (2002).	
	337	SKOLNICK and FETROW, "From genes to protein structure and function: novel applications of computational approaches in the genomic era," <u>Trends in Biotech.</u> , 18(1):34-39 (2000).	
4	338	STEIN and JOHNSON, "Lack of Neurodegeneration in Transgenic Mice Overexpressing Mutant Amyloid Precursor Protein is Associated with Increased Levels of Transthyretin and Activation of Cell Survival Pathways," <u>The Journal of Neuroscience</u> , 22(17):7380-7388 (September 1, 2002).	

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		Examiner Name	Sharon L. Turner
		Attorney Docket Number	15270J-004740US
Sheet	3	of	3

	339	TENNENT et al., "Serum amyloid P component prevents proteolysis of the amyloid fibrils of Alzheimer's disease and systemic amyloidosis," <u>PNAS</u> , 92:4299-4303 (1995).	
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